## DETAILED ACTION

**Claims 2 and 7-18 are presented for examination.**

Applicant's Amendment filed April 8, 2011 have been received and entered into the present application.

Claims 2 and 7-18 remain pending and under examination. No claims are amended.

Applicant's arguments, filed April 8, 2011, have been fully considered. Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

### *Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 7-13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of asthma, bronchitis, interstitial lung disease, insulin resistance, prediabetes, type 2 diabetes mellitus, metabolic syndrome, hypertension combined with hyperlipidemia or hypertension combined with atherosclerosis comprising the administration of telmisartan (or a salt thereof) with atorvastatin (or a salt thereof), does not reasonably provide enablement for the prevention of the same, for the reasons of record set forth at p.3-7 of the previous Office Action dated October 14, 2010, of which said reasons are herein incorporated by reference.

*Response to Applicant's Arguments*

Applicant traverses the instant rejection, stating that the Examiner refuses to follow *Ex parte Cho* when the distinctions between the case and the instant situation are insubstantial. Applicant insists that *Cho* should be followed because it is an example of how the law is correctly applied. Applicant further opines that Grundy acknowledges the complexity of metabolic syndrome, but asserts that the fact that the condition may be complex does not support a lack of enablement when the condition is well understood in the art. Applicant argues that, given that the claimed method of treatment of metabolic syndrome is admitted to be enabled, "it would follow that the method of prevention of metabolic syndrome would also be enabled regardless of the alleged "complex" nature of the syndrome" (p.4-5, Remarks). Applicant alleges that the specification provides extensive guidance as to how to prevent the claimed conditions by teaching that the combination(s) can be administered before patients are officially diagnosed and/or are suspected of having the claimed condition(s). Applicant cites to p.9-14 and 20-27 of the specification in support of his position that the disclosure provides guidance as to how to identify patients in need of the claimed method.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, Applicant again continues to cite the decision rendered in *Ex parte Cho* in support of his position, stating that it addresses the exact same issue on point here in the instant case. This is, and will remain, unpersuasive. The issue in *Cho* was that the Examiner had indicated a lack of enablement of various embodiments of the invention without providing an adequate explanation satisfying the initial burden of the examiner to show a lack of enablement. See p.7 of the *Cho* decision. This is *not*, contrary to Counsel's opinion, the exact same issue on point here under insubstantially different facts because the present Examiner has provided, in the context of the instant rejection, extensive discussion as to why the claims lack enabling guidance for the full scope of the claims. Applicant's attention is directed to p.2-8 of the Office Action dated November 26, 2008 for these reasons. This instant conclusion of a lack of

enablement *is not based upon unsupported assertions of a lack of enabling guidance as was the case in Cho*. Rather, the state of the prior art is clearly discussed in view of cited publications demonstrating the knowledge generally available in the art at the time of the invention taken in view of what is disclosed in the instant specification. Thus, the allegation that the exact same issue is addressed under insubstantially different facts continues to be a patent mischaracterization of the facts in the instant application versus those facts in the case under examination in *Cho* and is properly unpersuasive in this regard.

Moreover, in view of these clearly distinguishing facts of the instant case and the case under discussion in *Cho*, Applicant continues to ignore the urging from the Office to explain why the decision has any relevance to the instant application *in view of the supporting evidence provided in the instant rejection, as well as to provide a clear reason as to why the Office should be bound by a decision that is non-precedential in view of the clearly distinct fact patterns*. It is not understood as to why Applicant repeatedly continues to neglect to provide an answer to this query by the Office.

Secondly, Applicant opines that Grundy acknowledges the complexity of metabolic syndrome, but asserts that the fact that the condition may be complex does not support a lack of enablement when the condition is well understood in the art. This is, and will remain, unpersuasive. Not only does Grundy acknowledge the complexity of metabolic syndrome, he also expressly acknowledges that the art needs a better understanding of the link between insulin resistance and metabolic syndrome to provide improved management of the disease. See the abstract of Grundy, cited at p.5 of the Office Action dated November 25, 2008. Thus, while it may be true that the sheer complexity of a condition does not necessarily support a lack of enablement when the condition is well understood in the art, the fact remains that Grundy explicitly teaches that the condition *is not well understood in the art and, as such, a better and improved understanding is needed*. As a result, Applicant's position that the complexity of the condition does not support nonenablement when the condition is well understood is clearly faulty because the very teaching of Grundy is that the condition is *not* well understood in the art and, thus, the complexity and poor clinical

understanding of the condition contributes to the lack of enabling guidance of the claimed embodiment directed to "prevention".

Thirdly, Applicant argues that, given that the claimed method of treatment of metabolic syndrome is admitted to be enabled, "it would follow that the method of prevention of metabolic syndrome would also be enabled regardless of the alleged 'complex' nature of the syndrome". This is unpersuasive because Applicant has failed to advance any reasons or evidence to support his position that the enablement of "preventing" metabolic syndrome can be inferred from the ability of the claimed combination to "treat" metabolic syndrome. Statements of this nature are unsupported allegations and are clearly unpersuasive in accordance with the guidance provided at MPEP §2145, which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ 2d 1362 (Fed. Cir. 1997)".

Fourthly, and lastly, Applicant alleges that the specification provides extensive guidance as to how to prevent the claimed conditions by teaching that the combination(s) can be administered before patients are officially diagnosed and/or are suspected of having the claimed condition(s) and cites to p.9-14 and 20-27 of the specification in support of his position that the disclosure provides guidance as to how to identify patients in need of the claimed method. This is unpersuasive. Though Applicant provides guidance as to what parameters may indicate disruption and/or predisposition to particular conditions, the instant specification still provides no guidance to one of ordinary skill in the art to show that the instantly claimed combination actually functions to *prevent* the development of the claimed disorders in such patients. Without such evidence, the state of the art at the time of the invention as evidenced by the publication to Grundy clearly demonstrates that the objective of prevention would not have been reasonably expected by one of skill in the art and the lack of enabling guidance fails to rebut the clear unpredictability in the art with regard to this same objective.

For these reasons *supra*, and those previously made of record at p.3-7 of the Office Action dated

October 14, 2010, rejection of claims 2 and 7-13 is proper.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 and 7-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over De Gasparo et al. (WO 01/76573; 2001), in light of Robl et al. (U.S. Patent Application Publication No. 2002/001334; January 31, 2002), which is cited to show a fact, in view of Wienen et al. ("A Review on Telmisartan: A Novel, Long-Acting Angiotensin II-Receptor Antagonist", *Cardiovascular Drug Reviews*, 18(2); 2000:127-154), Cecil's Textbook of Medicine (2000), Harlan et al. (U.S. Patent Application Publication No. 2001/0006656; July 2001) and Bohm et al. (WO 02/15892; February 2002), each already of record, for the reasons of record set forth at p.7-13 of the previous Office Action dated October 14, 2010, of which said reasons are herein incorporated by reference.

*Response to Applicant's Arguments*

Applicant traverses the instant rejection, stating that stating that De Gasparo et al. fail to disclose the specific combination of telmisartan and atorvastatin anywhere in the reference. Applicant further alleges that De Gasparo et al. lists a number of commercially available sartans, including telmisartan, but fails to disclose this specific compound "as a selected compound in the context of a specific combination, much less with atorvastatin" (p.8, Remarks). In fact, Applicant submits that the only sartan mentioned in the reference in the context of a specific combination is valsartan, which Applicant alleges constitutes a teaching away from the use of telmisartan. Applicant makes the same allegations with regard to atorvastatin, stating that the compound is not mentioned in combination with telmisartan. Applicant submits that the secondary references, i.e., Wienen et al., Robl et al., Cecil's Textbook of Medicine, Harlan et al. or Bohm et al., do not provide motivation, reasonable expectation of success, or a teaching or suggestion of all of the claim limitations of the invention. Applicant particularly argues against the Wienen et al. reference because, despite these advantages attributed to telmisartan as mentioned by the Examiner, telmisartan was still not the most prescribed sartan for hypertension. Still further, Applicant submits that neither the primary nor the secondary references teach or suggest telmisartan increases the expression of genes regulated by the PPAR-$\gamma$ receptor, which is the reason that telmisartan is a preferred combination partner for atorvastatin in the treatment of, e.g., diabetes.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

In response, Applicant's attention is directed to p.8-13 of the Office Action dated October 14, 2010, which sets forth the teachings of De Gasparo et al. insofar as the reference expressly teaches the combination of an AT1-receptor antagonist in combination with an HMG-CoA reductase inhibitor (p.1, l.27-29), wherein the AT1-receptor antagonist may be selected from, *inter alia*, telmisartan (p.3, l.22) and the HMG-CoA reductase inhibitor may be selected from, *inter alia*, atorvastatin (p.5, l.9-11). De Gasparo et al. clearly contemplates embodiments of the invention wherein the combination of at least two

therapeutic components comprises an AT1-receptor antagonist (of which telmisartan is expressly disclosed as one of several interchangeable AT1-receptor antagonists that may be used in the context of the disclosed invention) or a pharmaceutically acceptable salt thereof, and an HMG-CoA reductase inhibitor (of which atorvastatin is expressly disclosed as one of several interchangeable HMG-CoA reductase inhibitors that may be used in the context of the disclosed invention) or a pharmaceutically acceptable salt thereof. Please reference p.1, p.3, l.22, and p.5, l.9-11 of De Gasparo et al. This teaching is clear, exact and unequivocally speaks to the contrary of Applicant's traversal that the reference fails to disclose the claimed combination.

Applicant appears to be of the persuasion that the lack of a specific example of the disclosed combination of telmisartan and atorvastatin somehow constitutes a complete lack of teaching of the claimed combination and/or constitutes a teaching away from the claimed combination in view of the fact that other combinations of agents are exemplified. This is not persuasive. A preferred or exemplified embodiment (in this case, compositions using valsartan) does not constitute a teaching away from other embodiments disclosed within the four corners of the reference, including non-preferred embodiments. Applicant is reminded that the disclosure of a reference must be considered as expansively as is reasonably possible to determine the full scope of the disclosure and, as a result, is most certainly not limited to that which is preferred and/or exemplified. Please see MPEP at §2123, which states, "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments…Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments." Thus, the fact that other compounds may be exemplified or preferred does not negate or direct the artisan away from the broader teaching of the reference, which expressly provides for, and, thus, clearly contemplates the use of, a combination of an AT1-receptor antagonist (i.e., telmisartan) with an HMG-CoA reductase inhibitor (i.e., atorvastatin). Moreover, Applicant is reminded that there is no legal requirement that a reference

*must exemplify* a particular embodiment in order to constitute a teaching of the same. A reference will constitute a teaching so long as the disclosure clearly describes and enables such an embodiment and, in the present case, such description is clearly found in De Gasparo et al.

Applicant's additional attempt to patentably distinguish the claimed invention over that of the prior art by asserting that neither the primary nor the secondary references teach or suggest that telmisartan increases the expression of genes regulated by the PPAR-γ receptor is, as before, not persuasive. The fact that Applicant has recognized another advantage of the combination of telmisartan and atorvastatin, when the prior art already acknowledges the desirability of this same combination for the identical therapeutic objectives as presently claimed, cannot be the basis for patentability. Please see *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In the instant case, even if De Gasparo et al., did not recognize the advantageous effect on increasing expression of genes regulated by PPAR-γ when telmisartan and atorvastatin were combined, the fact that Applicant has recognized this advantage is not considered a new therapeutic application because the known treatment of the same diseases as presently claimed using this combination of active agents was already known and recognized in the prior art. Though mechanisms of action of chemical entities are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability under 35 U.S.C. 102 and/or 103 is based upon the therapeutic applications and effects of the compounds, not the mechanism by which they exert such a therapeutic effect.

Applicant again states that "none of Wienen et al., Robl et al., Cecil's Textbook of Medicine, Harlan et al., or Bohm et al. provide what De Gasparo et al. lacks in providing to one of skill in the art as a motivation, reasonable expectation of success, or teaching or suggestion of all of the claim limitations of the claimed invention" (p.8, Remarks), which is also unpersuasive. The record clearly indicates that one

of ordinary skill in the art would have been motivated to combine the cited references in such a manner to render the presently claimed invention *prima facie* obvious with a reasonable expectation of success in making such a combination, absent factual evidence to the contrary, and Applicant has failed to provide any factual evidence to the contrary. Applicant's attention is directed to p.8-13 of the rejection presented in the previous Office Action dated October 14, 2010 for this reasoning, which will not be repeated herein so as not to burden the record.

Additionally, Applicant is again reminded that rejections made under 35 U.S.C. 103(a) are based upon the combination of references. As a result, focusing solely on the discrete teachings of each of the cited references is tantamount to examining each of them inside of a vacuum and fails to be persuasive in establishing non-obviousness because it is the *combined* teachings that are the basis for a proper conclusion of obviousness, not each individual reference alone. In other words, it must be remembered that the references are relied upon in combination and are not meant to be considered separately. To properly conclude obviousness of an invention *does not require the claimed invention to be expressly suggested in its entirety by any one single reference under 35 U.S.C. 103(a)*. Rather, the test is *what the combined teachings* of the references would have suggested to those of ordinary skill in the art. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Lastly, Applicant opines that, despite these advantages attributed to telmisartan as mentioned by the Examiner, telmisartan was still not the most prescribed sartan for hypertension. This argument is, and will remain, unpersuasive for two reasons: (1) Applicant fails to support his assertions that telmisartan is not the most prescribed sartan for hypertension by citing to factual documentation. Counsel's mere argument cannot take the place of evidence in the record. See MPEP §2145, which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)" and (2) even if,

*arguendo*, telmisartan was not the most prescribed sartan for hypertension (which the Examiner does not concede), the frequency with which it is prescribed does not negate the clear advantages, efficacy and low risk for drug interactions that telmisartan clearly has over other sartan compounds, which is evidenced by the teachings of Wienen et al. Therefore, one of ordinary skill in the art would have been motivated to select this sartan compound in particular due to these advantages, absent evidence to the contrary. The fact that telmisartan may not be the most preferred embodiment in the sense that it is not the most frequently prescribed sartan (which, it is repeated for the record, is an allegation by Applicant that is unsubstantiated by evidence), this does not teach away from the use of telmisartan *per se*. See MPEP §2123, which states, "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments…Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments."

For these reasons *supra*, and those previously made of record at p.7-13 of the Office Action dated October 14, 2010, rejection of claims 2 and 7-18 is proper.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14-18 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claim 18 of U.S. Patent Application No. 10/899,784 in view of De Gasparo et

al. (WO 01/76573; 2001), already of record, for the reasons of record set forth at p.15-17 of the previous Office Action dated October 14, 2010, of which said reasons are herein incorporated by reference.

The abandonment of copending U.S. Patent Application Nos. 10/757,015 and 11/300,947 renders the previously applied provisional rejections moot over such application(s).

*Response to Applicant's Arguments*

Applicant states that he will file a Terminal Disclaimer if (1) the instant claims be found otherwise allowable and (2) the copending claims pose a double patenting issue at that time. Applicant states that, since the scope of the claims may change and moot these rejections, there is no need to address these issues at this time.

Insofar as the instant claims are not presently in condition for allowance due to the tissues described *infra*, and further that the instant claims and the copending claims raise an issue under the judicially created doctrine of obviousness-type double patenting for the reasons previously set forth in the Office Action dated October 14, 2010 at p.15-17, the rejection remains proper and is maintained.

## ***Conclusion***

After extensive prosecution in this case, it appears that Applicants disagree with the Examiner's findings and that the disagreement is based on a point of law. In light of this, Applicants are reminded of their right to appeal the Examiner's rejections to the Board of Appeals and Interferences.

Rejection of claims 2 and 7-18 is proper.

No claims of the present application are allowed.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP §714.02 and §2163.06). Note that support should be provided for amendments to previously pending claims, as well as any newly

added claims. In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, not the published application. Due to the procedure outlined in MPEP §2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. §102 or 35 U.S.C. §103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims and share an inventor or assignee with the instant application. A copy of such copending claims is requested in response to this Office action in order to assist the examiner with double patenting analysis in the application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds Draper whose telephone number is (571)272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey S. Lundgren can be reached on (571)-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds Draper/
Primary Examiner, Art Unit 1629

June 17, 2011